Rejections under 35 USC §102

Claims 1-6 and 20-21 are rejected under 35 USC §102(a) as anticipated by Husmann et al. Applicants rebut the rejection on the grounds that each and every element of the claimed invention is not taught or implied by the reference. As is well-established, and stated in the MPEP at 706.02:

> "...for anticipation under 35 USC 102, the reference must teach each and every aspect of the claimed invention either explicitly or impliedly. Any feature not inherently taught must be inherently present."

In the present case, Husmann neither teaches nor suggests "a delivery unit comprised of at least one *synthetic* controlled release carrier material" (as required by the invention e.g., in claim 1 and new claim 20).

In contrast, Husmann discloses the use of Gelfoam, which is a specially treated porcine-derived gelatin product (EXHIBIT A). *This is not a synthetic material*, it is a natural material, and as such Hussman does not explicitly or inherently teach a "synthetic controlled release carrier material." The present anticipation rejection is therefore moot and applicants respectfully request that it be withdrawn.

Additionally, the claimed invention is directed to a method for delivering "therapeutic agents" to the ear to produce a therapeutic effect, for example, delivering gentamicin to treat tinnitus or other aural diseases. In contrast, the Husmann study uses Gelfoam to deliver gentamicin for the purpose of *causing nerve damage*. The quantity of gentamicin delivered, rate of delivery, and the method of delivery required for a *therapeutic* purpose is diametrically different from that required to *cause nerve damage*, therefore the Hussman reference not only does *not* anticipate the current invention, but it also does not make it obvious, since it teaches a method that would *not* enable one of skill in the art to practice the current invention with a *reasonable expectation of success*. In fact, since Husmann teaches nerve damage to the ear by the delivery of gentamicin using Gelfoam, one could reasonably suggest that the reference *teaches away* from the current invention (though applicants do not believe that the assertion of teaching away is strictly necessary or germane here, since Gelfoam is not equivalent to the synthetic controlled release carrier material of the present invention).

Such potential damage is additionally supported by explicit reference in product literature (supplied by Upjohn, the Gelfoam manufacturer) to adverse reactions caused when Gelfoam is used during tympanoplasty (EXHIBIT B). These adverse reactions include hearing loss. Clearly this would act as a disincentive to one of skill in the art to use Gelfoam as a material to deliver a therapeutic agent to the middle ear. Additionally, Gelfoam has been shown to be associated with fibrosis, neovascularization and epithelial metaplasia of the round window membrane when used for grafting (EXHIBIT C). Thus, not only does the Husmann reference not anticipate the present invention, but it also does not make obvious the present invention, in fact, it tends to support a finding of non-obviousness since it implies a lack of therapeutic success for the present invention, and could be seen as teaching away from the present invention. In view of the above facts and reasoning, applicants respectfully request that the rejection under 35 USC §102(a) be withdrawn.

Rejections under 35 USC §103

Claims 1-6, and 20-25 are rejected as anticipated by, or alternatively, obvious over Petrus in view of Kopke et al.

Applicants rebut the rejection on the grounds that the examiner has not established a prima facie case of obviousness because: 1) the combination of Petrus and Kopke would not make the invention obvious, absent impermissible hindsight reconstruction, because they do not, alone or in combination, teach or suggest all the claim limitations, and 2) neither would one of ordinary skill in the art, given the cited references, be led to believe that they could practice the invention with a reasonable expectation of success.

The legal standards for establishing a prima face case of obviousness is well-established and clearly set out in the MPEP at 706.02(j).

> "To establish a prima face case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation ...to modify or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be

found in the prior art and not [be] based on applicant's disclosure. In re Vaeck, 947 F.2d 488; 20 USPQ2d 1438 (Fed. Cir. 1991)."

In the present case, the combined references do not teach or suggest all the claim limitations. Specifically, the combined references do not teach a drug delivery unit comprised of a ...*controlled release carrier material*...*placed at least partially in the round window niche*.

The examiner's interpretation of the Petrus's disclosure is in error. The examiner asserts that "Petrus discloses the positioning of the drug delivery unit (4) in various locations in col. 6, lines 53-57, such as the middle ear (14)." This assertion is not factually correct. Petrus, confusing though it is, in fact only discloses placing a porous media in the "*proximal aspect of the external auditory canal* ...to deliver therapeutic agents to the tympanic cavity ...which includes the middle ear..." This means that the porous media is placed, at best, *on the ear drum, not in the middle ear and certainly not in the round window niche* (see attached figure), and that, somehow, drug is supposed to pass through the ear drum into the middle ear. Thus, Petrus does not disclose placing a carrier material in the round window niche. Kopke teaches using the "IntraEar" *catheter* (familiar to the applicants assignee (Durect Corporation) who is the assignee of the IntraEar patent portfolio) to deliver drug to the round window membrane, but does not teach or suggest using a controlled-release carrier material placed in the round window niche. Neither reference, alone or in combination, teach or suggest in any way that it may be advisable to place a drug delivery unit comprised of a controlled release carrier material at least partially in the round window niche. A catheter is quite different from a controlled release carrier material. They are different in structure, in method of use and in the way they work. They are not equivalents and are not suggestive of each other. A controlled release carrier material may be implanted using minimally invasive surgical techniques (Specification pp. 43-45) and retained in the round window niche without leaving a connecting tube connecting the inside of the middle ear to the outside environment. Other advantages are enumerated in the specification at pages 43-45 and 57-59.

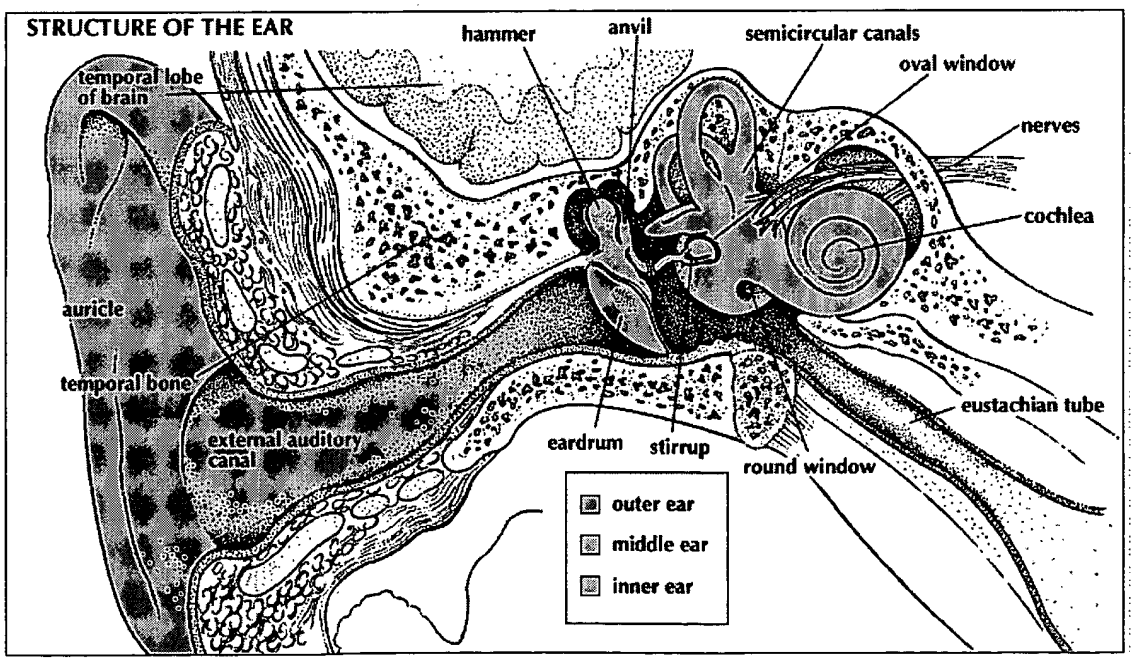
Although, in hindsight, the invention may *seem* quite simple, and perhaps obvious, it was not obvious at the time of the invention, and only the present disclosure makes it seem so. As eloquently stated by the Federal Circuit:

"To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher.' . . . One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." *In re Fine*, 5 USPQ2d 1596, 1600 (CAFC 1988) (quoting *W.L. Gore & Assocs. v. Garlock, Inc.*, 220 USPQ 303, 312-13 (CAFC 1983)).

and

"When determining obviousness, '[t]he invention must be viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time.'" *Diversitech Corp. v. Century Steps Inc.*, 7 USPQ2d 1315, 1318 (CAFC 1988) (quoting *Interconnect Planning Corp. v. Feil*, 227 USPQ 543, 551 (CAFC 1985)).

Additionally, placing a drug into the middle ear is not the same as or equivalent to placing a drug in the round window niche (and even if it were, Petrus would not suggest the present invention wherein a carrier material, not just a drug, is placed in the round window niche).



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As can be seen in the figure supplied, a drug placed in the middle ear (for example, a drug that was caused to pass through the ear drum into the middle ear) would tend to drain directly out of the middle ear through the Eustachian tube. It would not tend to pool in the round window niche. If enough drug were to be delivered to completely fill the middle ear, then it would certainly not be delivered in the controlled, accurate and predictable manner required to successfully practice the invention. One of the most important objects of the present invention is to provide a method for accurate delivery of small amounts of a drug over a period of time. This is particularly important since some of the drugs most commonly delivered, such as gentamicin, are ototoxic when given at inappropriately large doses, and are well-know to cause hearing loss.

If the method of Petrus were used to fill the middle ear cavity with such a drug, it would certainly not be delivered in the amount required for an effective and safe treatment. Therefore, one of skill in the art would not believe that he /she could practice the method of Petrus (whether or not combined with Kopke) with a reasonable probability of success to deliver a therapeutic agent, as currently claimed. The results that could be reasonably suggested by one or more disclosures must form part of an "obviousness" analysis, and in the present case, such results do not suggest success, but rather teach away from it, and therefore teach away from a finding of obviousness. As has been stated by the Federal Circuit:

> "An analysis of obviousness of a claimed combination must include consideration of the results achieved by that combination." *The Gillette Co. v. S.C. Johnson & Son*, 16 USPQ2d 1923, 1928 (CAFC 1990).
>
> and
>
> "Unless the [prior art] disclosures would have suggested to one of ordinary skill in the art at the time the invention was made that a [combination] should be so employed, [a] claim . . . is not unpatentable under 35 U.S.C. § 103." *In re Bond*, 15 USPQ2d 1566, 1569 (CAFC 1990).

In light of the above amendments and remarks, applicants submit that the present application is fully in condition for allowance, and request that the examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, applicants invite the examiner to contact applicants' attorney at (408) 864-7435.

Applicants believe that no fee is due with this communication, however, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge any additional fees required under 37 C.F.R. § 1.16 and 1.17, or credit any overpayment to Deposit Account No. **50-1953. A duplicate of this sheet is enclosed.**

Respectfully submitted,
DURECT CORPORATION

1 NOV 2001

Date:_____

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Adam Warwick Bell, D.Phil.
Reg. No. 43,490

10240 Bubb Road
Cupertino, California 95014
Phone: (408) 777-1417
Fax: (408) 777-3577